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# Accuracy of Biopsy and Cytology for the Preoperative Diagnosis of Colorectal Adenocarcinoma

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**Background and Objectives:** Endoscopic biopsy for the diagnosis of colorectal adenocarcinoma is not accurate in every case. Brush cytology can increase the sensitivity for the diagnosis of gastroesophageal lesions when combined with biopsy, but very little information is available for these techniques in the diagnosis of colorectal adenocarcinoma.

**Methods:** A retrospective medical records review of 110 patients was performed. All patients underwent a colorectal resection for primary adenocarcinoma after a diagnostic endoscopy. Biopsy and brush cytology was evaluated for their respective sensitivity. Seventy-three patients had both biopsy and cytology.

**Results:** The sensitivity of biopsy was 83.6% (92/110); for cytology, 78.1% (57/73; $P = 0.44$). From the 73 patients who had both diagnostic techniques, 68.5% (50/73) had both positive biopsy and cytology, 12.3% (9/73) only a positive biopsy, and 9.6% (7/73) only a positive cytology. The two techniques combined were not significantly superior to biopsy alone (90.4%, 66/73, vs. 80.8%, 59/73, respectively; $P = 0.16$), but tended to be superior to cytology alone ($P = 0.07$).

**Conclusions:** Cytology and biopsy have a comparable sensitivity. The combination of the two techniques compares favorably, but does not significantly increase the sensitivity of biopsy alone. Both techniques should be used whenever there are any uncertainties concerning the diagnosis of colorectal adenocarcinoma.

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KEY WORDS: **adenocarcinoma; cytology; biopsy; cancer; colorectal**

## INTRODUCTION

Colonoscopy is an important modality for the diagnosis and treatment of colorectal neoplasms. Colonoscopy has a sensitivity of 95% compared to 83% for barium enema. It is also more likely to detect smaller lesions and earlier-stage carcinoma [1]. The National Polyp Study Workgroup has reported that colonic polypectomy can decrease the incidence of colorectal cancer [2]. Furthermore, the American Cancer Society now recommends for the asymptomatic individual with no risk factors for colorectal cancer a sigmoidoscopy every 5 years beginning at age 50 [3]. Thus, we can expect an increase in use and demand for lower gastrointestinal endoscopy. Tissue diagnosis is important to exclude the presence of carcinoma in benign-appearing lesions. However, the accu-

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racy of biopsy is not perfect, and it has been reported that brush cytology can increase the positivity rate for colorectal cancer [4,5].

The role of cytology in the diagnosis of malignancy has been reported more frequently for upper gastrointestinal pathology than colorectal neoplasms [6–8]. These studies reveal that biopsy alone is inadequate for the diagnosis of malignancy in a significant proportion of patients. The present report evaluates the results of both cytology and biopsy for the diagnosis of colorectal adenocarcinoma. The sensitivity of biopsy and cytology performed during endoscopy is compared to the pathology of the resected colorectal specimens.

## MATERIALS AND METHODS

This is a retrospective medical records review of 110 patients who underwent resection of primary adenocarcinoma of the colon or rectum at Roswell Park Cancer Institute (RPCI) between 1 January 1994 and 31 December 1996. All patients had at least two to four biopsies or one brush cytology or both performed during a lower gastrointestinal endoscopy as part of the preoperative evaluation.

Tissue material from sigmoidoscopy or colonoscopy was compared with the pathology report from the resected surgical specimen. In some cases, patients were referred from outside hospitals, following a colonoscopy and tissue diagnosis. These patients were included in the analysis but only if the endoscopy was repeated, the lesions confirmed as being the one biopsied or brushed, and the pathology slides reviewed at RPCI. When tissue was obtained at an outside institution and RPCI, only the result from RPCI was included in the analysis. Every patient had a biopsy performed, including 80 patients at RPCI. Thirty patients had their outside pathology slides reviewed by our Pathology Department. In addition to the biopsy, cytology was available in 73 patients, including only 1 outside slide reviewed.

False negative sampling was defined as any biopsy or cytology not reported as malignant but with a confirmed carcinoma in the surgical specimen. Biopsies or cytologies that were reported to be "suspicious for malignancy but not conclusive" or severe dysplasia were not considered true positives. Since we specifically evaluated a group of patients with a final diagnosis of adenocarcinoma of the colon and rectum, by definition there were no false positive diagnosis possible. Statistical evaluation for comparison of the sensitivity of both biopsy and cytology was performed using the chi-square test. Results were considered statistically significant if $P < 0.05$.

## RESULTS

There were 110 patients, of whom 64 were males and 46 were females. The median age at diagnosis of the colorectal carcinoma was 64 years (range, 35–85). As illustrated in Table I, approximately two-thirds of the patients presented with rectal bleeding, diarrhea, or other change in bowel habits. The most common surgical procedures performed were low anterior resection (32 patients, 29.1%), abdominoperineal resection (28 patients, 25.5%), and right hemicolectomy (27 patients, 24.5%; Table II).

**TABLE I. Signs and Symptoms at the Time of Diagnosis**

| Clinical presentation | Number of patients[a] (%) |
|---|---|
| Rectal bleeding | 50 (45.5) |
| Change in bowel habits | 22 (20.0) |
| Abdominal pain | 15 (13.6) |
| Fecal occult blood | 15 (13.6) |
| Asymptomatic screening | 14 (12.7) |
| Rectal mass | 7 (6.4) |
| Nausea, vomiting | 5 (4.5) |

[a]Total patients, 110 (some patients presented with more than one sign or symptom).

The TNM staging of the resected specimens were as follows: 2 stage 0 (in situ), 36 stage I (tumor within bowel wall, negative lymph nodes), 32 stage II (tumor penetration through bowel wall, negative lymph nodes), 25 stage III (positive lymph nodes), and 15 stage IV (distant metastases). Eight cancers were well differentiated, 82 moderately differentiated, 14 poorly differentiated, and in 6 patients the histologic grade was not reported.

Biopsy was positive for adenocarcinoma in 92 of 110 patients, resulting in a sensitivity of 83.6%. Fifty-seven of 73 cytologies were diagnostic, for a sensitivity of 78.1% ($P = 0.44$).

In the 110 patients with a diagnosis of adenocarcinoma in the surgical specimen, both biopsy and cytology were obtained in 73 patients. In 68.5% (50/73), both techniques were positive. In 12.3% (9/73), only the biopsy was positive, and in 9.6% (7/73), only the cytology was positive. The sensitivity of combined biopsy and cytology was not statistically significantly different from biopsy alone (90.4%, 66/73, vs. 80.8%, 59/73, respectively; $P = 0.16$). Whereas the sensitivity of combined biopsy and cytology was not statistically significantly different from cytology alone, there was a trend (90.4%, 66/73, vs. 78.1%, 57/73; $P = 0.07$).

Ten biopsies and 12 cytologies revealed severe dysplasia. Should we have included severe dysplasia as diagnostic of malignancy, the sensitivity would have been better. The sensitivity of biopsy would be 92.7% (102/110), brushing 94.5% (69/73), with the two techniques having a combined sensitivity of 100%.

When the impact of an obstructing carcinoma was considered, there was no significant change in the sensitivity of the two techniques. However, in the presence of obstruction, there was a tendency for brush cytology to be more sensitive than in nonobstructing lesions, al-

**TABLE II. Type and Frequency of Surgical Procedures for Colorectal Adenocarcinoma**

| Surgery | Number of patients[a] (%) |
|---|---|
| Low anterior resection | 32 (29.1) |
| Abdominoperineal resection | 28 (25.5) |
| Right hemicolectomy | 27 (24.5) |
| Transanal excision | 8 (7.3) |
| Left hemicolectomy | 5 (4.5) |
| Pelvic exenteration | 5 (4.5) |
| Total proctocolectomy | 3 (2.7) |
| Total abdominal colectomy | 1 (0.9) |
| Sigmoid resection | 1 (0.9) |

[a]Total patients, 110.

though this was not statistically significant (100%, 10/10, vs. 74.6%, 47/63, respectively; $P = 0.10$; Table III). Obstruction was defined as an inability to pass the endoscope proximal to a cancer. Ulceration and the quality of the bowel preparation did not appear to have a negative impact on the sensitivity of the two techniques (Tables IV and V, respectively).

## DISCUSSION

The role of brushing cytology and biopsy has principally been evaluated for upper gastrointestinal tumors as opposed to colorectal cancer. For esophageal and gastric lesions, the sensitivity of biopsy has been reported between 72% and 92%. The sensitivity of brush cytology has generally ranged between 79% and 93% [5–7,9–13]. The majority of these reports concludes that the combination of cytology and histology clearly increases the sensitivity to as high as 97%–99% [6,9,12].

Our sensitivity for brush cytology and biopsy in the identification of colorectal adenocarcinoma was 78.1% and 83.6%, respectively. This difference was not statistically significant and we conclude that the two techniques have comparable accuracy. The combination of brush cytology and biopsy increased the sensitivity to 90.4%. The sensitivity of the combined techniques trends toward significance from the sensitivity of cytology alone ($P = 0.07$). It also compares favorably with the sensitivity of biopsy (80.8%) in patients who had the combined techniques (90.4%).

Leiman et al. [9] reported for upper gastrointestinal malignancies an accuracy of 83% for cytology and 84% for biopsy. They also reported that cytology correctly identified malignancy in 20% of cases where biopsy was inadequate or inconclusive. O'Donoghue et al. [6] compared cytology and biopsy in 394 patients with gastroesophageal malignancies. Cytology increased the diagnostic accuracy from 88.3% to 97.5%. Their false positive rate was 1.3% for cytology and less than 0.1% for biopsy. In this study, those cytology smears reported as suspicious for malignancy but not conclusive were included in the malignant group. In our series, inclusion of these cases would have increased the sensitivity of each technique above 90%, and the sensitivity of the combined techniques would have reached 100%.

**TABLE III. Sensitivity With and Without Complete Obstruction for Colorectal Adenocarcinoma**

| | No obstruction (%) | Complete obstruction (%) | |
|---|---|---|---|
| Cytology | 47/63 (74.6) | 10/10 (100) | $P = 0.10$ |
| Biopsy | 80/97 (82.5) | 11/13 (84.6) | $P = 0.10$ |
| | $P = 0.24$ | $P = 0.49$ | |

**TABLE IV. Colorectal Adenocarcinoma: Sensitivity With and Without Ulceration**

| | No ulceration (%) | Ulceration (%) | |
|---|---|---|---|
| Cytology | 22/32 (68.8) | 35/41 (85.4) | $P = 0.15$ |
| Biopsy | 43/56 (76.8) | 48/54 (88.9) | $P = 0.13$ |
| | $P = 0.45$ | $P = 0.76$ | |

**TABLE V. Sensitivity and Quality of the Bowel Preparation**

| | Excellent or good[a] (%) | Poor or fair[b] (%) | |
|---|---|---|---|
| Cytology[c] | 28/36 (77.8) | 14/20 (70.0) | $P = 0.54$ |
| Biopsy[d] | 41/49 (83.7) | 23/30 (76.7) | $P = 0.56$ |
| | $P = 0.58$ | $P = 0.74$ | |

[a]Excellent/good, greater than 80% of the mucosa visualized.
[b]Poor/fair, less than 80% of the mucosa visualized.
[c]In the remaining 17 patients bowel preparation was not reported.
[d]In the remaining 79 patients bowel preparation was not reported.

Winawer et al. [4] evaluated the impact of cytology in the diagnosis of colorectal cancer. Biopsy alone had a positive yield of 60%, whereas biopsy and cytology combined were positive for malignancy in 89% of patients. The morphology of the lesion was also important. The yield of positivity with biopsy was 33% for infiltrative lesions and 71% when the lesion was exophytic. No false positives were found. Watanabe et al. [10] reported a sensitivity of 86% for cytology and 76% for biopsy for the diagnosis of colorectal cancer.

The technical difficulties of sampling need to be addressed to understand why the accuracy of both biopsy and cytology is not optimal. Sometimes the anatomic location of the cancer makes it difficult to obtain a good angle and the biopsy needs to be taken tangentially. This is illustrated in a study by Leiman et al. [9], where the accuracy of cytology was higher than biopsy in the esophagus (89.8% vs. 77.8%, respectively) but less in the stomach, where it is easier to achieve a better angulation. O'Donoghue et al. [6] reported a statistically significant better sensitivity of biopsy over cytology, but only in the stomach. A stenotic or completely distorted colon may preclude an optimal approach to the tumor. The brush cytology has the advantage of being able to be introduced into a stenotic lesion and sample an area that cannot be

reached via biopsy. However, in our series we did not observe any statistically significant difference in the sensitivity of either technique when complete obstruction or ulceration were present.

Zargar et al. [5] reported 265 patients with a confirmed diagnosis in upper and lower gastrointestinal malignancies who underwent three different diagnostic modalities: biopsy, brush cytology, and aspiration cytology. The latter had an accuracy of 94% vs. 84.9% for brush cytology and 87.2% for biopsy. Aspiration cytology was markedly superior in the diagnosis of submucosal lesions and to a lesser degree for infiltrative and ulcerated lesions. Aspiration cytology provided the diagnosis in 21 of 24 lesions that were negative on both brush cytology and biopsy. Biopsy was highly accurate for polypoid lesions; however, for infiltrative lesions, brush cytology was more accurate.

A brush cytology can easily be obtained in the endoscopic suite and is associated with low morbidity. However, the sensitivity of cytology is dependent on the availability of an experienced cytopathologist and obtaining optimal diagnostic material on two slides with fixation. Another consideration in the choice of the tissue diagnosis technique is the cost. In our institute, the addition of brush cytology involves a supplement of $99.30 to the cost of diagnostic colonoscopy. A biopsy adds $252.30 to the total cost. Since the two techniques have comparable sensitivity, this must be taken into consideration when facing a typical colonic lesion that is suspicious for adenocarcinoma.

In summary, we strongly feel that both biopsy and brush cytology should be used whenever there are diagnostic and management considerations for colorectal adenocarcinoma, since the combination of the two increases sensitivity.

## REFERENCES


1. Rex DK, Rahmani EY, Haseman JH, et al.: Relative sensitivity of colonoscopy and barium enema for detection of colorectal cancer in clinical practice. Gastroenterology 1997;112:117–123.
2. Winawer SJ, Zauber AG, Ho MN, et al.: Prevention of colorectal cancer by colonoscopic polypectomy: The National Polyp Study Workgroup. N Engl J Med 1993;329:1977–1981.
3. Winawer S, Fletcher RH, Miller L, et al.: Colorectal cancer screening: Clinical guidelines and rationale. Gastroenterology 1997;112:594–642. (Published Errata: Gastroenterology 1997; 112:1060; and Gastroenterology 1998;114:625.)
4. Winawer SJ, Leidner SD, Hajdu SI, Sherlock P: Colonoscopic biopsy and cytology in the diagnosis of colon cancer. Cancer 1978;42:2849–2853.
5. Zargar SA, Khuroo MS, Mahajan R, et al.: Endoscopic fine needle aspiration cytology in the diagnosis of gastroesophageal and colorectal malignancies. Gut 1991;32:745–748.
6. O'Donoghue JM, Horgan PG, O'Donohoe MK, et al.: Adjunctive endoscopic brush cytology in the detection of upper gastrointestinal malignancy. Acta Cytol 1995;39:28–34.
7. Kobayashi S, Kasugai T: Brushing cytology for the diagnosis of gastric cancer involving the cardia and lower esophagus. Acta Cytol 1978;22:155–157.
8. Quizilbash AH, Castelli M, Kowalski MA, Churly A: Endoscopic brush cytology and biopsy in the diagnosis of cancer of the upper gastrointestinal tract. Acta Cytol 1980;24:313–318.
9. Leiman G, Tim L, Segal I: Diagnosis of upper gastrointestinal lesions by endoscopy, cytology and biopsy. S Afr Med J 1979; 55:619–623.
10. Watanabe H, Munazawa M, Shoji K, et al.: Diagnosis of early cancer of the colon and rectum. Tohoku J Exp Med 1979;129: 183–195.
11. Zargar SA, Khuroo MS, Jan GM, et al.: Prospective comparison of the value of brushings before and after biopsy in the endoscopic diagnosis of gastroesophageal malignancy. Acta Cytol 1991;35: 549–552.
12. Behmard S, Sadeghi A, Bagheri SA: Diagnostic accuracy of endoscopy with brushing cytology and biopsy in upper gastrointestinal lesions. Acta Cytol 1978;22:153–154.
13. Bron B, Massih L, Brahime G, et al.: Etude prospective de dépistage des tumeurs digestives par l'endoscopie: Comparaison do la cytologie par brossage et de l'histologie. Schweiz Med Wschr 1979;209:610–612.
14. Parker S, Tong T, Bolden S, Wingo P: Cancer statistics, 1997. Ca Cancer J Clin 1997;47:5–27.